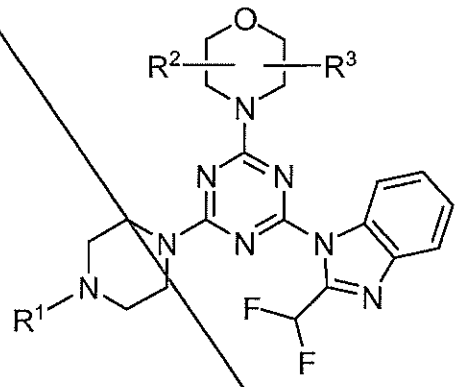
Claims

1. A compound of formula (I)



(I)

wherein

R^1 is methyl, n-hexyl, aminoethyl, methylaminoethyl, ethylaminoethyl, dimethylaminoethyl, acryloylaminoethyl, methacryloylaminoethyl, methoxyethyl, ethoxyethyl, C_1-C_4-alkyl-sulfonyl, acryloyl, or methacryloyl; or R^1 is aminoethyl, acryloyl or acryloylaminoethyl carrying a linker and a tag, and

R^2 and R^3, independently of each other, are hydrogen or C_1-C_4-alkyl, or R^2 and R^3 together form an ethylene bridge;

and tautomers, solvates and pharmaceutically acceptable salts thereof.

2. The compound of formula (I) according to claim 1 wherein

R^1 is methyl, n-hexyl, 2-aminoethyl, 2-(methylamino)ethyl, 2-(ethylamino)ethyl, 2-(acryloyl-amino)ethyl, 2-methoxyethyl, 2-ethoxyethyl, C_1-C_4-alkylsulfonyl, acryloyl, or methacryloyl.

3. The compound of formula (I) according to claim 1 wherein

R^1 is 2-aminoethyl, acryloyl or 2-(acryloylamino)ethyl, each carrying a linker and a tag.

4. The compound of formula (I) according to claim 1 wherein

R^1 is methyl, 2-aminoethyl, 2-(acryloylamino)ethyl, 2-ethoxyethyl, methylsulfonyl, ethylsulfonyl, iso-propylsulfonyl, acryloyl, or methacryloyl.

5. The compound of formula (I) according to claim 1 wherein

R^1 is methyl, 2-aminoethyl, 2-(acryloylamino)ethyl, 2-ethoxyethyl, methylsulfonyl, ethylsulfonyl, or acryloyl.

6. The compound of formula (I) according to claim 1 wherein R^1 is methyl, 2-(acryloylamino)ethyl, methylsulfonyl, or acryloyl.

7. The compound of formula (I) according to claim 1 wherein R^1 is 2-aminoethyl or acryloyl, each carrying a linker and a tag selected from biotin, a fluorophore or a polymeric bead.

8. The compound of formula (I) according to any one of claims 1 to 7 wherein R^2 and R^3, independently of each other, are hydrogen, methyl, ethyl, or isopropyl, or R^2 and R^3 together form a methylene or an ethylene bridge.

9. The compound of formula (I) according to any one of claims 1 to 7 wherein R^2 and R^3 are both hydrogen, one hydrogen and one methyl, or both methyl, or form together an ethylene bridge.

10. The compound of formula (I) according to any one of claims 1 to 7 wherein R^2 is (*S*)-2-methyl, (*R*)-2-methyl, (*R*)-3-methyl, or (*S*)-3-methyl, and R^3 is hydrogen, or R^2 and R^3 are (2*R*,6*S*)-2,6-dimethyl, (2*R*,6*R*)-2,6-dimethyl, (2*R*,3*R*)-2,3-dimethyl, (2*S*,5*S*)-2,5-dimethyl, (3*S*,5*R*)-3,5-dimethyl, (3*S*,5*S*)-3,5-dimethyl, a 2,5-ethylene bridge, a 2,6-ethylene bridge, a 3,5-ethylene bridge, or both hydrogen.

11. The compound of formula (I) according to claim 1 wherein R^1 is methyl, n-hexyl, 2-aminoethyl, 2-(acryloylamino)ethyl, 2-ethoxyethyl, methylsulfonyl, ethylsulfonyl, or acryloyl, and R^2 and R^3 are hydrogen.

12. The compound of formula (I) according to claim 1 wherein R^1 is methyl, 2-(acryloylamino)ethyl, methylsulfonyl, or acryloyl, and R^2 and R^3 are hydrogen.

13. The compound of formula (I) according to claim 1 wherein R^1 is methyl or methylsulfonyl, and R^2 and R^3 are hydrogen.

14. A pharmaceutical composition comprising a compound of formula (I) according to any one of claim 1 to 13.

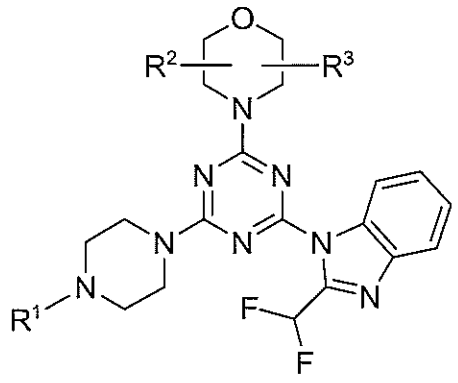
15. Use of a compound of formula (I) according to any one of claim 1 to 13 in the manufacture of a medicament for preventing or treating a disease or disorder modulated by PI3 kinases and/or mTOR.

16. Use of a compound of formula (I) according to any one of claim 1 to 13 in the manufacture of a medicament for treating a hyperproliferative disorder.

17. A method of screening for compounds binding to a lipid kinase comprising
(a) binding a compound of formula (I), wherein R^1 is aminoethyl, acryloyl or acryloylaminoethyl carrying a linker and a tag, to a lipid kinase;
(b) mixing with a compound to be screened for binding to said lipid kinase;
(c) measuring displacement of said compound of formula (I) based on the property of the tag; and
(d) calculating binding of the compound to be screened from the result of the measured displacement.

Claims

1. A compound of formula (I)



(I)

wherein

R^1 is methyl, n-hexyl, aminoethyl, methylaminoethyl, ethylaminoethyl, dimethylaminoethyl, acryloylaminoethyl, methacryloylaminoethyl, methoxyethyl, ethoxyethyl, C_1-C_4-alkylsulfonyl, acryloyl, or methacryloyl; or R^1 is aminoethyl, acryloyl or acryloylaminoethyl carrying a linker and a tag, and

R^2 and R^3, independently of each other, are hydrogen or C_1-C_4-alkyl, or R^2 and R^3 together form an ethylene bridge;

and tautomers, solvates and pharmaceutically acceptable salts thereof,

with the exception of the compounds wherein R^1 is methylsulfonyl and R^2 and R^3 are hydrogen or R^2 and R^3 together form an ethylene bridge.

2. The compound of formula (I) according to claim 1 wherein

R^1 is methyl, n-hexyl, 2-aminoethyl, 2-(methylamino)ethyl, 2-(ethylamino)ethyl, 2-(acryloylamino)ethyl, 2-methoxyethyl, 2-ethoxyethyl, C_1-C_4-alkylsulfonyl, acryloyl, or methacryloyl.

3. The compound of formula (I) according to claim 1 wherein

R^1 is 2-aminoethyl, acryloyl or 2-(acryloylamino)ethyl, each carrying a linker and a tag.

4. The compound of formula (I) according to claim 1 wherein

R^1 is methyl, 2-aminoethyl, 2-(acryloylamino)ethyl, 2-ethoxyethyl, methylsulfonyl, ethylsulfonyl, iso-propylsulfonyl, acryloyl, or methacryloyl.

5. The compound of formula (I) according to claim 1 wherein
R^1 is methyl, 2-aminoethyl, 2-(acryloylamino)ethyl, 2-ethoxyethyl, methylsulfonyl, ethylsulfonyl, or acryloyl.

6. The compound of formula (I) according to claim 1 wherein
R^1 is methyl, 2-(acryloylamino)ethyl, methylsulfonyl, or acryloyl.

7. The compound of formula (I) according to claim 1 wherein
R^1 is 2-aminoethyl or acryloyl, each carrying a linker and a tag selected from biotin, a fluorophore or a polymeric bead.

8. The compound of formula (I) according to any one of claims 1 to 7 wherein
R^2 and R^3, independently of each other, are hydrogen, methyl, ethyl, or isopropyl, or R^2 and R^3 together form a methylene or an ethylene bridge.

9. The compound of formula (I) according to any one of claims 1 to 7 wherein
R^2 and R^3 are both hydrogen, one hydrogen and one methyl, or both methyl, or form together an ethylene bridge.

10. The compound of formula (I) according to any one of claims 1 to 7 wherein
R^2 is (*S*)-2-methyl, (*R*)-2-methyl, (*R*)-3-methyl, or (*S*)-3-methyl, and R^3 is hydrogen, or R^2 and R^3 are (2*R*,6*S*)-2,6-dimethyl, (2*R*,6*R*)-2,6-dimethyl, (2*R*,3*R*)-2,3-dimethyl, (2*S*,5*S*)-2,5-dimethyl, (3*S*,5*R*)-3,5-dimethyl, (3*S*,5*S*)-3,5-dimethyl, a 2,5-ethylene bridge, a 2,6-ethylene bridge, a 3,5-ethylene bridge, or both hydrogen.

11. The compound of formula (I) according to claim 1 wherein R^1 is methyl, n-hexyl, 2-aminoethyl, 2-(acryloylamino)ethyl, 2-ethoxyethyl, ethylsulfonyl, or acryloyl, and R^2 and R^3 are hydrogen.

12. The compound of formula (I) according to claim 1 wherein R^1 is methyl, 2-(acryloylamino)ethyl, or acryloyl, and R^2 and R^3 are hydrogen.

13. The compound of formula (I) according to claim 1 wherein R^1 is methyl and R^2 and R^3 are hydrogen.

14. A pharmaceutical composition comprising a compound of formula (I) according to any one of claim 1 to 13.

15. Use of a compound of formula (I) according to any one of claim 1 to 13 in the manufacture of a medicament for preventing or treating a disease or disorder modulated by PI3 kinases and/or mTOR selected from cancer, stroke, diabetes, hepatomegaly, cardiovascular disease, Alzheimer's disease, cystic fibrosis, autoimmune diseases, atherosclerosis, restenosis, psoriasis, allergic disorders, inflammation, neurological disorders, a hormone- related disease, conditions associated with organ transplantation, immunodeficiency disorders, destructive bone disorders, proliferative disorders, infectious diseases, conditions associated with cell death, thrombin-induced platelet aggregation, chronic myelogenous leukemia (CML), liver disease, pathologic immune conditions involving T cell activation, and CNS disorders.

16. Use of a compound of formula (I) according to any one of claim 1 to 13 in the manufacture of a medicament for treating cancer.

17. A method of screening for compounds binding to a lipid kinase comprising
(a) binding a compound of formula (I), wherein R^1 is aminoethyl, acryloyl or acryloylaminoethyl carrying a linker and a tag, to a lipid kinase;
(b) mixing with a compound to be screened for binding to said lipid kinase;
(c) measuring displacement of said compound of formula (I) based on the property of the tag; and
(d) calculating binding of the compound to be screened from the result of the measured displacement.